CLAIMS

1. A method for producing nonhuman mammalian embryos comprising the following steps:

(a) evaluate and/or determine the asynchrony of development (T) between two embryos of the same species and of the same age:

(i) the first embryo being produced by crossing at the time t_0 a male, preferably vasectomized, with a female who has preferably received hormone treatment to increase ovulation, the said first embryo being at least cultured and/or manipulated *in vitro*;

(ii) the second embryo being produced by crossing at the time t_0 a fertile male with a female who has preferably received hormone treatment in order to increase ovulation, said second embryo being normally fertilized and obtained by parthenogenetic activation,

the evaluation and/or determination taking place at the latest on the day of uterine implantation of said second embryo, and;

(b) transfer an embryo which is at least cultured and/or manipulated *in vitro* into the uterus of a recipient female who was crossed with a vasectomized male at the time $t = t_0 + T$ (+/- 25% T);

(c) optionally, allow said embryo transferred in step b) to become implanted and to develop in the uterus of said recipient female.

2. The method as claimed in claim 1, characterized in that said first embryo is cultured and/or manipulated *in vitro* at the latest up to the day of implantation.

3. The method as claimed in claims 1 and 2, characterized in that the evaluation and/or determination is carried out at a stage of development chosen from the 1 cell stage, 2 cell stage, 4 cell

stage, 8 cell stage, 16 cell stage, morula stage and blastocyst stage.

4. The method as claimed in claim 3, characterized in that the evaluation and/or determination is carried out at the blastocyst stage.

5. The method as claimed in claims 1 to 4, characterized in that the evaluation and/or determination of the asynchrony of development T is carried out by cell counting.

6. The method as claimed in claims 1 to 5, characterized in that said asynchrony of development T is at least 15 hours.

7. The method as claimed in claim 6, characterized in that said asynchrony of development T is 24 hours.

8. The method as claimed in claims 1 to 7, characterized in that said embryo transferred in step b) is cultured under the same conditions as said first embryo.

9. The method as claimed in claims 1 to 8, characterized in that said embryo transferred in step b) is at the 1 cell stage.

10. The method as claimed in claims 1 to 8, characterized in that said embryo transferred in step b) is at the 2 cell stage.

11. The method as claimed in claims 1 to 8, characterized in that said embryo transferred in step b) is at the 4 cell stage.

12. The method as claimed in claims 1 to 11, characterized in that said transferred embryo develops into a fetus.

13. The method as claimed in claim 12, characterized in that said fetus develops into a newborn.

14. The method as claimed in claims 1 to 13, characterized in that said embryo cultured and/or manipulated *in vitro* is a transgenic embryo.

15. The method as claimed in claims 1 to 13, characterized in that said embryo cultured and/or manipulated *in vitro* is a reconstituted embryo obtained by nuclear transfer.

16. The method as claimed in claims 1 to 13, characterized in that said embryo cultured and/or manipulated *in vitro* is a reconstituted transgenic embryo obtained by nuclear transfer.

17. The method as claimed in claims 1 to 16, characterized in that said mammal is selected from rodents, lagomorphs, hoofed animals, equine animals and primates, except humans.

18. The method as claimed in claim 17, characterized in that said mammal is a rodent selected from mice, rats, hamsters, guinea pigs.

19. The method as claimed in claim 17, characterized in that said hoofed animal is selected from bovines, ovines, caprines and porcines.

20. The method as claimed in claim 17, characterized in that said lagomorph is rabbit.

21. An embryo of a mammal, except humans, and/or fetus, newborn, adult mammal, or cells derived therefrom, produced by a method comprising or including the method as claimed in one of claims 1 to 20.

22. An embryo of a transgenic mammal, except humans, and/or fetus, newborn, adult mammal, or cells derived therefrom, produced by a method comprising or including the method as claimed in one of claims 1 to 20.

23. An embryo of a mammal, except humans, reconstituted *in vitro* obtained by nuclear transfer, and/or fetus, newborn, adult mammal, or cells derived therefrom, produced by a method comprising or including the method as claimed in one of claims 1 to 20.

24. A progeny of said adult mammal as claimed in claims 21 to 23.

25. An *in vitro* method for cloning the mammal by nuclear transfer comprising or including a method as claimed in any one of claims 1 to 20.

26. A method for producing rabbit embryos comprising the following steps:

(a) evaluate and/or determine the asynchrony of development (T) between two rabbit embryos of the same age:

- the first embryo being produced by crossing at the time t_0 a male, preferably vasectomized, with a female who has preferably received hormone treatment to increase ovulation, said first embryo being at least cultured and/or manipulated *in vitro*;
- the second embryo being produced by crossing at the time t_0 a fertile male with a female who has preferably received hormone treatment in order to increase ovulation, the second embryo being normally fertilized and obtained by parthenogenetic activation;

the evaluation and/or determination taking place at the latest on the day of uterine implantation of said second embryo normally fertilized or obtained by parthenogenetic activation; and

(b) transfer a rabbit embryo which is cultured and/or manipulated *in vitro*, no older than the blastocyst stage into the uterus of a recipient female who was crossed with a vasectomized male at the time t = t_0 + T (+/- 25% T);

(c) optionally, allow said embryo transferred in step b) to become implanted and to develop in the uterus of said recipient female.

27. The method as claimed in claim 26, characterized in that the evaluation and/or the determination is carried out at a stage of development between days D1 and D7 *post coitum*.

28. The method as claimed in claim 27, characterized in that the evaluation and/or determination is carried out on day D5 post coitum.

29. The method as claimed in claims 26 to 28, characterized in that said asynchrony of development T is 23 hours +/- 25%.

30. The method as claimed in claims 26 to 29, characterized in that said embryo cultured and/or manipulated *in vitro* is a transgenic embryo.

31. The method as claimed in claims 26 to 29, characterized in that said embryo cultured and/or manipulated *in vitro* is a reconstituted embryo obtained by nuclear transfer.

32. The method as claimed in claims 26 to 29, characterized in that said embryo cultured and/or manipulated *in vitro* is a reconstituted transgenic embryo obtained by nuclear transfer.

33. The method as claimed in claims 26 to 32, characterized in that said embryo transferred in step b) is at the 1 cell stage.

34. A rabbit embryo and/or fetus, newborn, adult rabbit, or cells derived therefrom, produced by a method comprising or including the method as claimed in one of claims 26 to 33.

35. A transgenic rabbit embryo and/or fetus, newborn, adult rabbit or cells derived therefrom, produced by a method comprising or including the method as claimed in one of claims 26 to 33.

36. An *in vitro* reconstituted rabbit embryo obtained by nuclear transfer and/or fetus, newborn, adult rabbit, or cells derived therefrom, produced by a method comprising or including the method as claimed in one of claims 26 to 33.

37. A progeny of said adult rabbit as claimed in claims 34 to 36.

38. An *in vitro* method for cloning of rabbits by nuclear transfer comprising or including the method as claimed in any one of claims 26 to 33.

39. An *in vitro* method for cloning rabbits by nuclear transfer, comprising the steps of:

a) inserting a rabbit donor cell or a rabbit donor cell nucleus into a rabbit enucleated oocyte under conditions which make it possible to obtain a reconstituted embryo;

b) activating the reconstituted embryo obtained in step a);

c) transferring said reconstituted embryo into a surrogate rabbit, such that the reconstituted

embryo develops into a fetus, and possibly into a newborn;

and is characterized in that the method comprises or includes a method as claimed in any one of claims 26 to 33.

40. The method as claimed in claim 39, characterized in that the transfer of nucleus into the recipient cytoplasm is carried out by fusion of the donor cell and of the recipient cytoplasm.

41. The method as claimed in claim 39, characterized in that the transfer of nucleus into the recipient cytoplasm is carried out by microinjection of the donor nucleus into the recipient cytoplasm.

42. The method as claimed in claim 39, characterized in that said activation phase during *in vitro* culture is carried out by adding simultaneously, successively or spaced out over time, to the culture medium for said reconstituted embryo, at least one protein kinase inhibitor and at least one inhibitor of protein synthesis.

43. An *in vitro* method for cloning mammals, except humans, comprising the steps of:

a) inserting a donor cell or a donor cell nucleus into an enucleated oocyte of a mammal of the same species or of a species different from that of the donor cell under conditions which make it possible to obtain a reconstituted embryo;

b) activating the reconstituted embryo obtained in step a);

c) transferring said reconstituted embryo into a surrogate female mammal, such that the reconstituted embryo develops into a fetus, characterized in that said activation is carried out by adding simultaneously, successively or spaced out over time, to the culture medium for

said reconstituted embryo, at least one protein kinase inhibitor and at least one inhibitor of protein synthesis.

44. The method as claimed in claim 43, characterized in that said mammal is selected from rabbits, rodents, in particular rats, mice, and from bovines, ovines, caprines, porcines, equines, primates, with the exception of humans.

45. The method as claimed in claim 42 to 44, characterized in that said protein kinase inhibitor is 6-DMAP and said inhibitor of protein synthesis is cycloheximide (CHX).

46. Method for producing a recombinant protein by a transgenic animal comprising the step of producing an embryo of a nonhuman mammal as claimed in claims 1 to 20.

47. A method for producing a recombinant protein by a transgenic rabbit comprising the step of producing a rabbit embryo as claimed in claims 26 to 33.

48. The use of a transgenic animal capable of being obtained by the method as claimed in claims 1 to 20 or of a transgenic rabbit capable of being obtained by the method as claimed in claims 26 to 33 as a model for studying human pathologies.

49. The use of a transgenic animal capable of being obtained by the method as claimed in claims 1 to 20 or of a transgenic rabbit capable of being obtained by the method as claimed in claims 26 to 33 for the production of recombinant proteins.

50. The use according to claim 49, characterized in that said recombinant protein is produced in the milk of the transgenic animal.